

## Morphine in Acute Chest Infections

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[To the Editor of the BRITISH MEDICAL JOURNAL]

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SIR,—The observation of "T. G." (April 22, p. 958) about the lethal effect of morphine injections in patients suffering from chest trouble is recognized in the literature. Thus in Goodman and Gilman's *the Pharmacological Basis of Therapeutics* (p. 205) we find the sentence: "The use of morphine in bronchial asthma is often dangerous and has caused death." The intention has been to ease the patient's breathing and give him a good night's rest. Morphine, however, should be employed only with the greatest possible restraint. Probably it is better never to use it in these cases at all. It depresses respiration by its action on the respiratory centre, so that its effect may be the opposite of easing breathing. It abolishes the cough reflex, thus favouring the accumulation of bronchial secretions; it also exerts a definite but slight bronchospastic effect<sup>1</sup> which would only tend to make the asthma worse. Piness<sup>2</sup> reported 15, Balyeat<sup>3</sup> 5, and Unger<sup>4</sup> 2 deaths in cases of status asthmaticus following morphine injections.

In a lecture delivered at St. Mary's Hospital during 1949 Dr. Leon Unger, of Chicago, restated the thesis in his book<sup>5</sup> that in his opinion morphine was definitely contraindicated in asthma: since giving up its use he had had no deaths occurring in acute asthmatic attacks in 15 years. There may be some confusion about the use of morphine in asthma because it is often used beneficially in the nocturnal dyspnoea of left ventricular failure. This so-called "cardiac asthma" is quite different from the allergic bronchial asthma under discussion.

An explanation of the action of morphine in bronchial asthma may be its property of releasing histamine from various tissues. Sir Thomas Lewis had already shown that in man an intracutaneous injection of morphine produces the triple response, indicating the release of H-substance (i.e., histamine) from the epithelial cells. The release of histamine by morphine has recently been directly demonstrated by us<sup>6 7</sup> in isolated perfused mammalian tissue. This property is shared by codeine, thebaine, apomorphine, and papaverine, which with morphine must all be classed as powerful "histamine liberators." It is interesting to note in this connexion that codeine is also apt to cause weals at the site of injection and marked anaphylactic reactions after its intravenous use (see Goodman and Gilman, loc. cit., p. 204), although generally it is considered to be one of the safest opium alkaloids.

The released histamine may be disastrous on account of its action on smooth muscles, heart, and capillary endothelium, resulting in broncho-constriction, bronchial oedema, or general circulatory collapse. But this does not explain why some patients with chest trouble are particularly sensitive to morphine. Such patients may either release histamine after morphine more readily and in greater amounts than normally, or they may be hypersensitive to the histamine itself, or both factors may operate. The fact that morphine and other opium alkaloids are powerful histamine liberators has obvious clinical implications, not only in bronchial asthma but perhaps also in any condition with an allergic basis. Furthermore, the anti-histamine drugs may prove effective therapeutic agents when signs of collapse occur after a morphine injection.—We are, etc.,

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